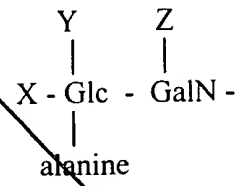
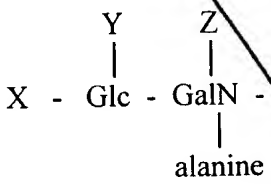


wherein X is selected from the group consisting of glucose, glucose-rhamnose and H;
wherein Y is selected from the group consisting of rhamnose and H; and
wherein Z is selected from the group consisting of glucose and H; and
a pharmaceutically acceptable carrier.

26. (Amended) A composition of matter comprising
a covalent conjugate of a non-toxic lipid and a polysaccharide comprising



wherein X is selected from the group consisting of glucose, glucose-rhamnose and H; Y is selected from the group consisting of rhamnose and H; and Z is selected from the group consisting of glucose and H.

REMARKS

Applicant has amended claims 14 and 26. Claims 14-43 are pending. No new matter has been added.

Rejection of Claims 14-43 Under 35 U.S.C. §112, Second Paragraph

Claims 14-43 have been rejected under 35 U.S. C. §112, second paragraph, as being indefinite for three reasons set forth by the Examiner.

It has been asserted that claims 14-22 and 24 are indefinite because of the term "therapeutically effective amount". Applicant has amended claim 14 to add the limitation that the therapeutically effective amount is one which is effective to increase CFTR expression.

Support for the amendment can be found throughout the application and in particular on page 3, lines 7-9.

Claim 26 and the claims dependent thereon have been rejected because of the use of the term "biocompatible". Applicant has amended claim 26 to delete the phrase incorporating the word biocompatible and to insert the word non-toxic as the limitation on the lipid. Support for this amendment is found throughout the application and in particular on page 12, lines 28-30. The sentence on page 12 teaches that the polysaccharide is attached to a non-toxic, lipophilic anchor that is biocompatible with the human subject. It is Applicant's belief that the term "biocompatible with the human subject" is clear on its face. In order to advance prosecution, Applicant has amended the claim to clarify that this phrase relates to a non-toxic lipid.

Claims 14-43 have been rejected because, according to the Examiner, the claims may "be inclusive of fatty acid portions of LPS structure". Applicant disagrees. The LPS core moiety is defined on pages 7-9 of the specification. The definition discloses the basic structural component of the LPS core moiety and teaches that the core may be the entire core of the LPS "which consists essentially of the polysaccharide portion free of the lipid tail (which is somewhat toxic)" or may be fragments thereof. It is clear from this language that the LPS core moiety includes the polysaccharide portion of LPS but not the lipid tail.

Rejection of Claims 26-43 Under 35 U.S.C. §102

Claims 26-43 have been rejected under 35 U.S.C. §102 as being anticipated by Masoud et al. According to the Examiner, Masoud et al. teaches the isolation of LPS "core" of *P. aeruginosa* and that the core contains an alanine. The Examiner indicates that the terms "bioactive agent" and "covalent conjugate" in the claims are interpreted broadly to include the lipo portions of the LPS.

Masoud et al. demonstrates the core structure for LPS obtained from *P. aeruginosa* serotype 06 IATS mutant strain A 28 in figures 8 and 9. Also shown in figure 9 are the core structures previously illustrated by Drewry et al., Rowe and Meadow, and Kropinski et al. The discussion teaches that only partial and tentative structures for the core from LPS of serologically distinct strains of *P. aeruginosa* belonging to serotypes 02, 03, and 05 were proposed. These were the ones shown in figure 9. It further teaches that an accurate chemical structure for this region has not yet been reported.

Claims 26-43 are not anticipated by Masoud et al. because the compositions claimed therein encompass a covalent conjugate of the polysaccharide core with either a non-toxic lipid or a bioactive agent. Claim 36 recites a covalent conjugate of a bioactive agent and a polysaccharide having the core presented in the claim. As set forth in the specification on page 13, a bioactive agent includes diagnostic agents and molecules effecting the metabolism of a cell expressing a CFTR, including peptides, nucleic acids, and other natural and synthetic drug molecules. The Masoud et al. reference includes several proposed or tentative core structures of *P. aeruginosa* on page 6724 of the reference. Although the reference describes core structures there is no suggestion or indication in the reference that the core structure binds to CFTR. Part of the claimed invention is based on this discovery. Because it was discovered that the core structure of LPS interacts with CFTR, it was discovered that therapeutic compositions containing this structure, conjugated to a non-toxic lipid or a bioactive agent could be prepared and delivered to a subject for therapeutic purposes. The reference does not suggest conjugation of the core region to a lipid or bioactive agent.

Rejection of Claims 14-23 and 25 Under 35 U.S.C. §103

Claims 14-23 and 25 have been rejected under 35 U.S.C. §103 as being unpatentable over Masoud et al. in view of Pennington et al. According to the Examiner, Pennington teaches the preparation of an LPS vaccine from *P. aeruginosa* but does not teach LPS of the claim structure. Since, according to the Examiner, Masoud discloses the core LPS claimed, it would have been obvious to one of ordinary skill in the art to use Masoud's core in the vaccine of Pennington. It is stated that "one of ordinary skill in the art would have been motivated to apply Masoud et al's isolated *P. aeruginosa* LPS to Pennington et al.'s vaccine in order to create species specific vaccine for *P. aeruginosa* vaccine".

Pennington et al. performed a study to determine whether a cross-protective core glycolipid antigen vaccine might provide pulmonary protection against several unrelated gram-negative bacilli, including *P. aeruginosa*. In the study, a vaccine derived from the J-5 mutant of *E. coli* 0111 was used and animals were challenged with *P. aeruginosa*, *E. coli*, and Klebsiella Pneumoniae. The data demonstrated that only weak cross-protection against pseudomonas pneumoniae was detected in the recipients of the J-5 vaccine. No protection against pneumonia due to either *E. coli* or Klebsiella was observed. The vaccine used in the Pennington reference is

the heptavalent LPS cell wall preparation used previously in the guinea pig model. The LPS preparation was from the *P. aeruginosa*. The other vaccine preparation used was the core glycolipid antigen of the J-5 mutant of *E. coli*. That vaccine was a heat-killed, whole-cell vaccine.

There is no suggestion in the Pennington reference that the core polysaccharide moiety of LPS would produce an effective vaccine. Since Pennington uses the whole LPS molecule and Masoud does not suggest that the partial core structure would be therapeutic, it would not have been obvious to use the structure disclosed in Masoud as a vaccine for *P. aeruginosa*.

Allowable Subject Matter

Applicant thanks the Examiner for the indication that claim 24 is free of the prior art.

Summary

It is believed that each of the pending claims is now in condition for allowance. If the Examiner has any questions, he is encouraged to contact Applicant's representative at the number listed below.

Respectfully submitted,

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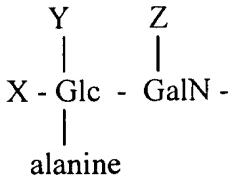
Docket No. B00801/70155
Date: August 27, 2002
X08/27/02

MARKED-UP CLAIMS

14. (Amended) A pharmaceutical preparation comprising

a therapeutically effective amount of a CFTR expression regulator for upregulating CFTR expression, wherein the CFTR expression regulator is a polysaccharide that is an LPS core moiety comprising



wherein X is selected from the group consisting of glucose, glucose-rhamnose and H;

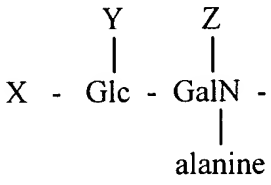
wherein Y is selected from the group consisting of rhamnose and H; and

wherein Z is selected from the group consisting of glucose and H; and

a pharmaceutically acceptable carrier.

26. (Amended) A composition of matter comprising

a covalent conjugate of a non-toxic lipid [biocompatible with a human subject] and a polysaccharide comprising



wherein X is selected from the group consisting of glucose, glucose-rhamnose and H; Y is selected from the group consisting of rhamnose and H; and Z is selected from the group consisting of glucose and H.